

Original Article

Breast cancer characteristics in Mongolian and disparities of ethnicities among Chinese patients

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Abstract: Purpose: This work was to analyze breast cancer (BC) characteristics of Mongolian patients, summarize main BC characteristics of minority ethnicities and compare with that of Mainland China. Methods: BC main characteristics of Mongolian and Han from Inner Mongolia of China from 2011 to 2014 were collected and analyzed. BC patients of Chinese from Central China and USA were enrolled for comparable analysis. BC characteristics of minority ethnicities from other reports of China were searched and compared with that of Mainland China. Results: There were no disparities of BC characteristics between Mongolian and Han in three groups of patients of China (Mongolian and Han patients in Inner Mongolia and Central China). BC characteristics of the three groups of China showed significant differences of that in Chinese American, including higher proportion of younger patients, larger tumor size, lymph node positive, regional stage, hormone receptor (HR) negative and human epidermal growth factor receptor 2 (HER2) positive ($p < 0.001$) for China. BC characteristics were reported in only four minority ethnicities of China, including Hui, Uygur, Mongolian and Kazakh. Compared with Mainland China, main BC characteristics of the patients among Mongolian, Hui and Kazakh in China displayed similar patterns, but with distinct patterns with that of Uygur, including lower rates of localized stage, lymph node negative and ER positive. Conclusion: BC characteristics of Mongolian were similar with that of Han in China, but not for Chinese American. BC characteristics of Mongolian, Hui and Kazakh were similar with that of Mainland China, but not for Uygur patients.

Keywords: Breast cancer, characteristics, Mongolian, Chinese patient, race/ethnicity, China

Introduction

Breast cancer (BC) is a common malignancy and major health threat throughout women's whole lives [1]. BC is a heterogeneous disease, with different characteristics in different geographies, ethnicities and socio-economical status [2]. For example, in the US, as compared with non-Hispanic (NH) white patients, NH black women displayed several distinct characteristics, including lower proportion of stage I, higher rate of the triple-negative subtype, and higher incidence and mortality rate [3-6]. In our recent study [7], BC main characteristics in Mainland China showed distinct patterns from Chinese patients in other developed areas and USA, including significant younger onset age, lower proportion of patients with early stage,

lymph node negative, small tumor size and ER positive. These distinct patterns may warrant appropriate different preventive and treatment strategies in China [7].

BC incidence in China is increasing in the past two decades [8, 9]. BC characteristics of Chinese displayed distinct patterns in different periods and socio-economical regions [8, 9]. However, BC characteristics among minority ethnicities of China have rarely been systematically reported. The minority ethnicities of China accounted approximate 8.5% of Chinese Population based on the sixth national census in 2010 of China. Therefore, a comprehensive understanding of BC characteristics among minority ethnicities is essential for designing effective preventive and therapeutic strategies.

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Table 1. BC Characteristics of Chinese patients among Inner Mongolia, Central China and USA

Item	Mongolian	Han of Inner Mongolia	Central China	Chinese American	P value
	Number (%)	Number (%)	Number (%)	Number (%)	
Age					
<40	13 (16.5)	23 (17.7)	125 (12.5)	147 (6.4)	<0.001
40-54	38 (48.1)	63 (48.5)	519 (51.8)	858 (37.6)	
55-69	22 (27.8)	36 (27.7)	271 (27.0)	810 (35.5)	
>69	6 (7.6)	8 (6.2)	87 (8.7)	468 (20.5)	
Tumor size					
≤2 cm	29 (36.7)	38 (29.2)	281 (28.0)	1,403 (61.5)	<0.001
2<T≤5 cm	39 (49.4)	76 (58.5)	625 (62.4)	726 (31.8)	
T>5 cm or T4	11 (13.9)	16 (12.3)	96 (9.6)	154 (6.7)	
Lymph node					
Positive	35 (44.3)	62 (47.7)	458 (45.7)	627 (27.5)	<0.001
Negative	44 (55.7)	67 (51.5)	520 (51.9)	1,655 (72.5)	
Unknown	0 (0)	1 (0.8)	24 (2.4)	1 (0.04)	
Stage					
Stage I	20 (25.3)	25 (19.2)	211 (21.1)	1,173 (51.4)	<0.001
Stage II	49 (62.0)	72 (55.4)	508 (50.7)	886 (38.8)	
Stage III	10 (12.7)	33 (25.4)	283 (28.2)	224 (9.8)	
Pathological type					
Invasive ductal carcinoma	70 (88.6)	120 (92.3)	946 (94.4)	1,980 (86.7)	<0.001
Invasive lobular carcinoma	3 (3.8)	3 (2.3)	13 (1.3)	128 (5.6)	
Others	6 (7.6)	7 (5.4)	43 (4.3)	175 (7.7)	
Grade					
Grade I	17 (21.5)	11 (8.5)	80 (8.0)	425 (18.6)	<0.001
Grade II	43 (54.4)	84 (64.6)	606 (60.5)	975 (42.7)	
Grade III	10 (12.7)	17 (13.1)	138 (13.8)	742 (32.5)	
Unclassified or Unknown	9 (11.4)	18 (13.8)	178 (17.8)	141 (6.2)	
Molecular subtype					
HR+/HER2-	41 (51.9)	75 (57.7)	513 (51.2)	1,494 (65.4)	<0.001
HR+/HER2+	8 (10.1)	13 (10.0)	99 (9.9)	237 (10.4)	
HR-/HER2+	10 (12.7)	15 (11.5)	167 (16.7)	175 (7.7)	
HR-/HER2-	17 (21.5)	24 (18.5)	219 (21.9)	207 (9.1)	
Unknown	3 (3.8)	3 (2.3)	4 (0.4)	170 (7.4)	

HR: hormone receptor. HER2: human epidermal growth factor receptor 2.

This work first compared the main BC characteristics of Mongolian with Han patients among Inner Mongolia, Central China and USA. Then we summarized the main BC characteristics of minority ethnicities reported in recent ten years, and compared with that in Mainland China reported previously [7].

Patients and methods

Patients

Characteristics of BC patients from Inner Mongolia Autonomous Region People's Hospital in

Northern China and Renmin Hospital of Wuhan University in Central China were collected from Jan 2011 to Dec 2014. BC patients with localized and regional stage (stage I to III) were enrolled mainly for surgical procedure. BC patients with metastasis were suggested to the Department of Oncology. So the patients with stage I to III were selected for analysis. Major characteristics for each patient were obtained from the medical records and the stage was performed based on the American Joint Committee on Cancer (AJCC) staging criteria version 7. Finally, a total of 209 cases of invasive female BC patients in Inner Mongolia of China

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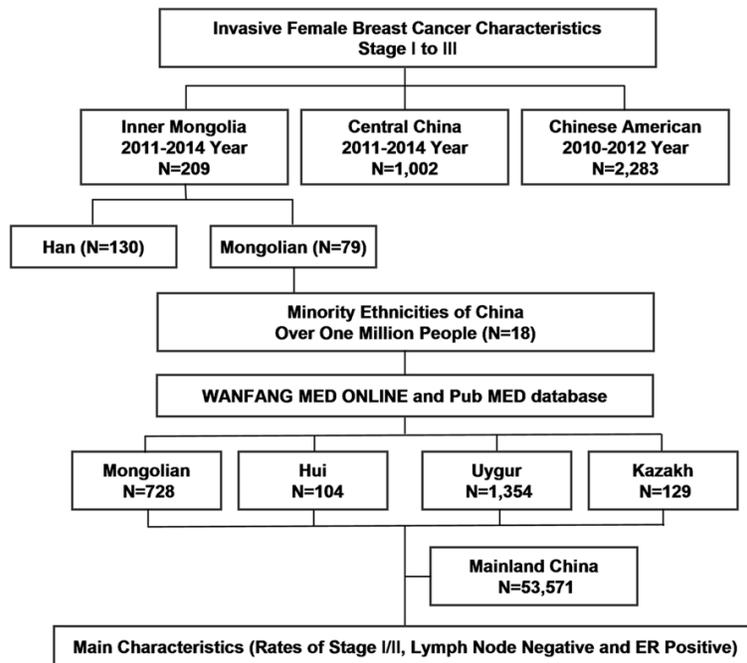


Figure 1. Schematic of patient selection.

were identified, with 75 cases of Mongolian and 130 cases of Han. Additionally, a total of 1,002 female BC Han patients with stage I to III were selected from Central China for comparable analysis.

BC Characteristics of Chinese American from the US were selected from the latest database of Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) (SEER*Stat Database: Incidence-SEER 18 Regs Research Data+Hurricane Katrina Impacted Louisiana Cases, Nov 2014 Sub (1973-2012 varying)-Linked To County Attributes-Total U.S., 1969-2013 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2015, based on the November 2014 submission). The permission SEER ID of the internet access for the database was 11960-Nov2014. We used the SEER*Stat (Version 8.2.1) software to extract the data. And invasive female BC patients with stage I to III of Chinese American from 2010 to 2012 were identified as described previously [7].

BC characteristics of the patients from Inner Mongolia, Central China and Chinese American were listed in **Table 1**. The schematic of patient selection was illustrated in **Figure 1**. This study

protocol was approved by the Institutional Ethics Committee of Renmin Hospital of Wuhan University.

BC characteristics of minority ethnicities from other reports of China

Eighteen minority ethnicities of China with population over one million based on the Tabulation on the 2010 population census of China were selected, including Zhuang, Hui, Manchu, Uygur, Miao, Yi, Tujia, Tibetan, Mongolian, Dong, Buyi, Yao, Bai, Korean, Hani, Li, Kazakh, and Dai. BC characteristics of reports for these minorities have been searched based on WANFANG MED ONLINE and Pub MED database since 2005. Data was updated at January 2016.

If several reports were from the same hospital and the same period, only the report with longer time periods was selected. Characteristics reported by numbers simply or separately in some reports were adopted after conversion.

Statistical analysis

BC patients were divided into four age groups: <40 years, 40-54 years, 55-69 years and >69 years. Characteristics among Inner Mongolia, Central China and Chinese American were compared using the Chi-square test. Differences of BC characteristic between Mainland China and minority ethnicities were also analyzed using the Chi-square test. The Chi-square test was performed on SPSS software version 17.0 (SPSS Inc. Chicago, IL) and $P < 0.05$ was considered statistically significant.

Results

Comparison of BC characteristics among patients of Mongolian, Han and Chinese American

Median ages for 79 Mongolian patients and 130 Han patients from Inner Mongolia, and 1,002 Han patients from Central China, were 50 years (range 27-86 years), 49 years (29-78

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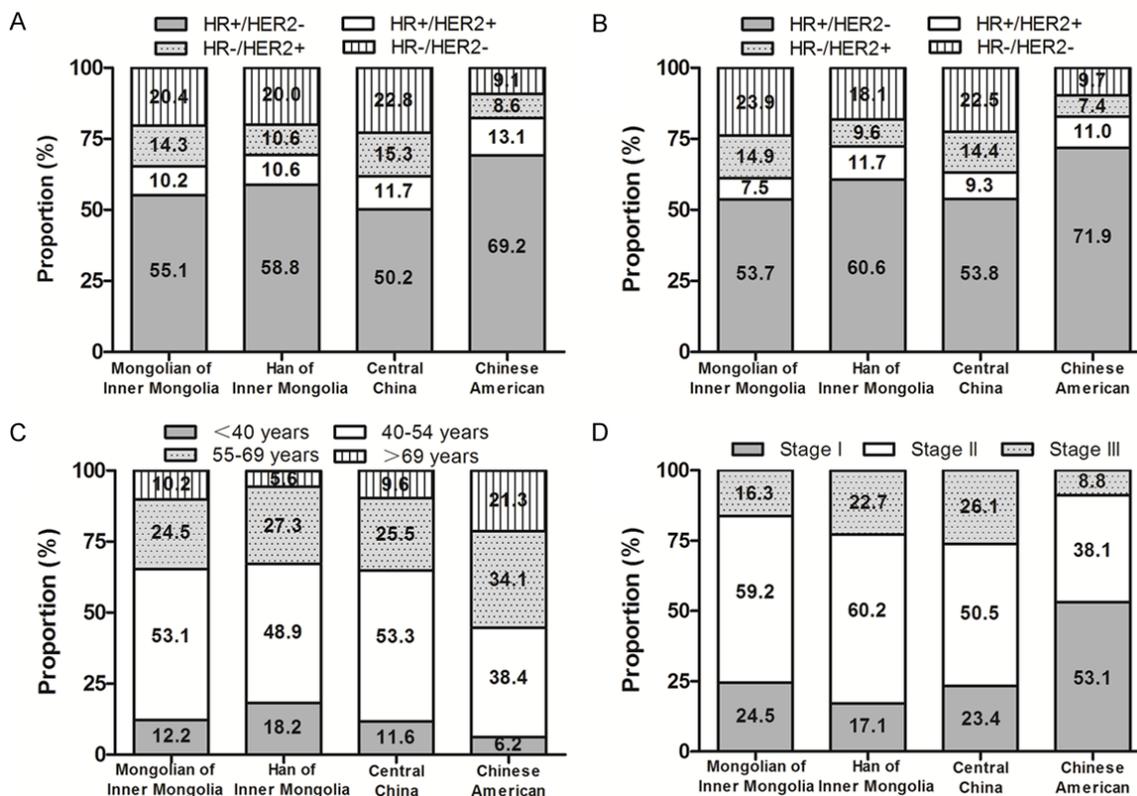


Figure 2. Relationships of molecular subtypes with age and stage of BC patients among Inner Mongolia, Central China, and Chinese American. Proportional differences of molecular subtypes in younger (<55 years old) patients (A), and localized stage (stage I and II) patients (B); Age (C) and stage (D) distributions among different groups of patients in HR positive BC patients.

years) and 50 years (18-89 years), respectively. A total of 2,283 Chinese patients with stage I to III of invasive female BC from USA were selected for comparable analysis. BC characteristics of patients from Mongolian and Han patients in Inner Mongolia, Central China and Chinese American were listed in **Table 1**. Over 60% of the patients in the three groups of China (Mongolian and Han patients in Inner Mongolia and Central China) were less than 55 years old, which were significant higher than that in Chinese American (44.0%, Chi-square test, $P < 0.001$). Likewise, there were significant higher patients with larger tumor size, lymph node positive, regional stage (Stage III), hormone receptor (HR) negative and human epidermal growth factor receptor 2 (HER2) positive among the Chinese patients from China than that from USA (Chi-square test, $P > 0.001$). Notably, there were significant higher patients with poorly differentiated grade (Grade III) in Chinese American group than that in the other three groups from China. Further analysis showed no signifi-

cant differences among the three groups of China (Chi-square test, $P > 0.05$), although Mongolian patients displayed lower proportion of stage III and higher proportion of well differentiated grade (Grade I).

Relationships of molecular subtypes with age and stage among BC Chinese patients

Then we further compared the differences of molecular subtypes among Chinese patients with younger (age <55 years old) and localized stage (stage I and II). As shown in **Figure 2A**, the proportions of molecular subtypes among the patients of Inner Mongolia and Central China displayed similar pattern (Chi-square test, $P > 0.05$). But these patterns were significantly different from Chinese American, including higher proportions of HR+/HER2- and HR+/HER2+, and lower proportions of HR-/HER2+ and HR-/HER2- (Chi-square test, $P < 0.001$). Likewise, the molecular subtypes of patients with localized stage showed similar results as

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Table 2. Summarization of BC characteristics in different ethnicities of China

Ethnicity	Periods	Number	Median Age	Younger age rate	Stage I/II rate	Lymph node negative rate	ER positive rate
Mongolian	2011.1-2014.12 (This study)	79	50	62.0	87.3	55.7	62.0
	1990.1-2007.12 [10]	649	49	NP	51.8	NP	58.4
Subtotal	1990-2014	728	49.1	62.0	55.7	55.7	58.8
Hui	2000.1-2007.6 [11]	104	46	NP	NP	55.0	62.5
Uygur	2005.2-2009.9 [12]	264	NP	83.0	59.1	36.4	70.1
	2008.1-2014.1 [13]	294	NP	77.6	59.1	NP	49.0
Kazakh	2003-2010 [14]	85	NP	88.2	NP	32.9	60.0
	2007.1-2013.8 [15]	284	46	76.8	NP	NP	59.2
	2004.1-2008.12 [16]	427	NP	NP	NP	37.5	49.2
Subtotal	2000-2014	1,354	46	79.9	59.1	36.6	56.0
Kazakh	2004.1-2014.10 [17]	129	46	NP	66.2	51.6	71.0
Mainland China	1995-2012 [7]	53,571	49.3	NP	66.0	52.5	61.7

Younger age: age <55 years old. NP: not provided.

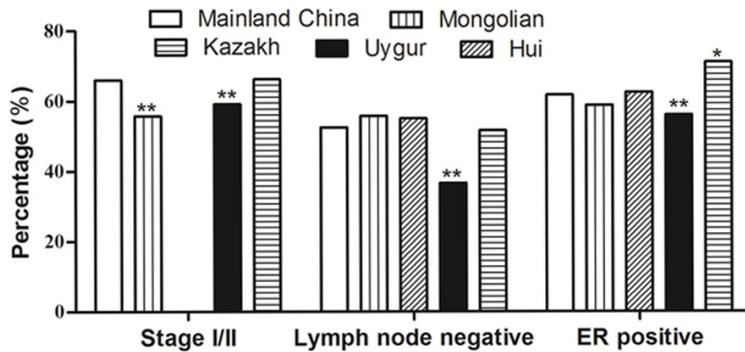


Figure 3. Main characteristics distribution of patients among Mongolian, Hui, Uygur, Kazakh and Mainland China. As compared with the patients of Mainland China, the differences of characteristics for each ethnicity displayed statistical significance (**: $P < 0.01$; *: $P < 0.05$).

that in younger Chinese patients between China and USA (Figure 2B). Furthermore, we compared the differences of age and stage distributions in HR positive patients. As shown in Figure 2C, the proportions of age groups among the HR positive patients in Inner Mongolia and Central China displayed similar pattern with over 60% younger patients (<55 years old). While in Chinese American, approximately 60% patients of HR positive were older than 55 years old. In HR positive patients, over 50% of the patients in China were stage II, and the proportions of patients with stage I in China were significantly lower than that in Chinese American (Figure 2D, Chi-square test, $P < 0.001$). But there were no significant differences of stage distributions among the three groups of China (Figure 2D, Chi-square test, $P > 0.05$).

BC characteristics of minority ethnicities in China

Based on the database, BC characteristics were reported in only four minority ethnicities of China, including Hui, Uygur, Mongolian and Kazakh [10-21]. There was only one study for each ethnicity of Hui, Mongolian and Kazakh [10, 11, 17]. There were nine studies for Uygur. We only selected five studies for comparable analysis because of repeated information or unavailable information of other reports [18-

21]. Main BC characteristics of Hui, Uygur, Mongolian and Kazakh, in combination with this study of Mongolian and Mainland China of our previous work [7], were summarized in Table 2. For each ethnicity, the values of characteristics were obtained by weight calculation of the reports.

A total of 2,134 BC patients of these four minority ethnicities were enrolled from 1990 to 2014 in three Autonomous regions of China (Xinjiang, Inner Mongolian and Ningxia). Median ages at diagnosis between Mongolian and Mainland China were similar, while higher than that of the other three minority ethnicities. And the proportion of younger BC patients (<55 years old) of Uygur was significant higher than that of Mongolian (Chi-square test, $P < 0.001$).

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Other main BC characteristics, including the rates of Stage I/II, lymph node negative and ER positive, were also illustrated in **Figure 3**. As comparable with Mainland China, BC characteristics of Mongolian and Hui displayed similar rates of lymph node negative and ER positive, but significantly lower rate of Stage I/II of Mongolian. And the three main characteristics of Uygur were all significant lower than that of Mainland China. BC characteristics of Kazakh displayed similar rates of Stage I/II and lymph node negative, but significantly higher rate of ER positive.

Discussion

Disparities of BC characteristics are common for BC heterogeneities, and partly due to the factors such as race/ethnicity, geographies, genetic, environmental and socio-economical status [1-8]. Therefore, BC characteristics of minority ethnicities of China should be comprehensively understood for conducting appropriate preventive and treatment strategies for these patients. In this study, we first analyzed BC characteristics of Mongolian in Inner Mongolia of China and compared with that of Han in Inner Mongolia and Central China in the same period. The results showed no characteristic disparities of the patients between Mongolian and Han. Then BC characteristics of the three groups of China were compared with that of Chinese American. As compared with Chinese American, BC patients among Mongolian and Han of China displayed more aggressive patterns, including younger onset age, lower proportion of localized stage and ER positive and higher proportion of HER2 positive. These results warranted appropriate preventive and treatment strategies in China as described in our previous work [7].

Mongolians are mainly distributed in northern China, Mongolia and Russia. Unfortunately, there were rare studies reported BC characteristics of Mongolian. One study reported that BC incidence in Mongolia was lower than that of other Asian countries, with approximate one third of incidence rate in China [22]. And the potential unique factors for disparities might be unusual diet (primarily red meat and dairy) in addition to genetics and environment compared with other Asian countries. However, BC characteristics of Mongolian in this study

showed no disparities with Han patients of China. One of the main potential reasons is the change of lifestyle in the process of industrialization from traditional pastoral lifestyle to sedentary lifestyle, as that emerging in most areas throughout the industrialization and urbanization of China.

In order to understand the disparities of BC characteristics among different ethnicities, in combination with this study, we conducted a retrospective review of main BC characteristics for other minority ethnicities. Then we compared the disparities of main characteristics with that of Mainland China reported in our recent study, which enrolled over 50,000 invasive BC patients. It is regrettable that there were few unique reports of BC characteristics for minority ethnicities in China. Only four ethnicities were enrolled and only one single-center study was for Hui and Kazakh. BC patients among Mongolian, Hui and Kazakh displayed similar main BC characteristics with that of Mainland China, other than the significant lower rate of localized stage for Mongolian and significant higher rate of ER positive for Kazakh. The lower proportion of localized stage for Mongolian may be in part due to that the other larger report was from a less developed area not like the capital of Hohhot in Inner Mongolia of this study [10]. Additionally, this larger study covered long time periods from 1990 to 2007, which may display different BC pattern in different time periods. In this study, the patients between Inner Mongolia and Central China were from the same periods and displayed the similar BC characteristics. The reasons for higher ER positive of Kazakh were partly due to the small cohort size, ethnicity, lifestyle and environment, which need to be investigated in the future.

Nine studies reported BC characteristics of Uygur in Xinjiang province of China. For comparable analysis, four studies with repeated information from the same hospital or unavailable information of main characteristics were not included in the analysis [18-21]. BC characteristics of Uygur displayed significant disparities as compared with that of Mainland China, including lower rates of localized stage, lymph node negative and ER positive. These patterns showed more patients of Uygur with aggressive BC and worse prognosis, indicating early diag-

nosis and intensive treatment, as reported in other studies [12, 16, 19-21]. Unfortunately, the proportion of younger patients (<55 years old) were significant higher than that of Mongolian and Central China. The reasons might be physiological conditions, education level, psychological status and diet [23]. Moreover, the genetic disparity may be another important factor, such as higher rate of BRCA1 [24] and CYP19 gene polymorphisms [25] reported in recent studies.

HER2 status is one of important indicators for BC prognosis and treatment selection. HER2 positive rates were similar between Mongolian and Han in China in this study, while significant higher than Chinese American. HER2 status in the other reports of minority ethnicities was unavailable or unconfirmed by fluorescence in situ hybridization (FISH) [10-13, 18, 20, 21], which was not summarized for comparable analysis. But the median HER2 positive rate of Uygur patients reported from several studies was 30.6% (15.3%-34.8%) [12, 14-16, 19], which were higher than that of Han population in this study. A recent multicenter study of China evaluated HER2 status in large cohort patients by immunohistochemistry (IHC) and FISH [26]. HER2 positive rate of patients in Han population (27.1%) was significant higher than that of patients in Miao ethnicity (20.0%), but lower than that of patients in Man (38.5%) and Hui (33.3%) ethnicities, indicating paramount disparities among ethnic population of China [26].

We acknowledge several limitations of this study. First, a multicenter study with larger cohort patients of Mongolian should be enrolled and followed up. Second, the inherent disparities among Mongolian, Han and Chinese American should be further investigated. Third, detailed characteristics and larger cohort patients from other minority ethnicities need to be investigated. Additionally, other important BC characteristics, such as family history, reproductive history, treatment strategies and survival analysis also needs to be investigated in further study, which are clearly important in evaluating the disparities of intrinsic biological behaviors, as well on the formulating preventive and therapeutic strategies.

In summary, this study demonstrated similar patterns of BC characteristics of the patients

between Mongolian and Han population in China, but paramount disparities of Chinese patients between China and USA. BC characteristics of minority ethnicities in China were rarely reported in most ethnicities. Compared with Mainland China, main BC characteristics of the patients among Mongolian, Hui and Kazakh displayed similar patterns, but with distinct patterns with that of Uygur, including lower rates of Stage I/II, lymph node negative and ER positive. Future studies with larger cohort, more ethnicities and detailed characteristics should be conducted to design effective preventive and therapeutic strategies for minority ethnicities of China.

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Disclosure of conflict of interest

None.

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